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Leukaemia Section

Short Communication

t(6;11)(q24.1;p15.5) NUP98/CCDC28A

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Abstract

Review on t(6;11)(q24.1;p15.5), with data on the genes involved

KEYWORDS
Chromosome 6; chromosome 11; Acute megakaryoblastic leukemia; T lymphoblastic leukaemia/lymphoma

Clinics and pathology

Disease

Acute megakaryoblastic leukemia (M7 AML) and T lymphoblastic leukemia

Epidemiology

Only two cases to date: a 5-year-old female patient (Tosi et al, 2005) and a 26-year-old male patient (Romana et al, 2006).

Cytogenetics

Cytogenetics molecular

FISH technique with the NUP98 probe and BAC RP11-900M13 probe has been used to confirm the translocation in the reported case (Romana et al, 2006).

Additional anomalies

The T-ALL adult patient showed an additional abnormality of 12p13 (Romana et al, 2006).

Genes involved and proteins

CCDC28A (coiled-coil domain containing 28A)

Location
6q24.1

Protein
CCDC28A encodes a coiled-coil domain containing protein. The native CCDC28A protein has no recognizable similarity to other proteins or functional domains, and no function has so far been assigned to the coiled-coil domain, leaving the biological function of CCDC28A undetermined.

NUP98 (nucleoporin 98 kDa)

Location
11p15.4

Note
also known as C6orf80 and MGC131913

Protein
NUP98 belongs to the nucleoporin gene family and encodes a 186 kDa precursor protein that undergoes autoproteolytic cleavage to produce a 98 kDa nucleoporin and 96 kDa nucleoporin. The 98 kDa nucleoporin contains a Gly-Leu-Phe-Gly repeat domain and participates in many cellular processes including nuclear import/export, mitotic progression, and regulation of gene expression. The

96 kDa nucleoporin is a component of the nuclear pore complex.

Result of the chromosomal anomaly

Hybrid gene

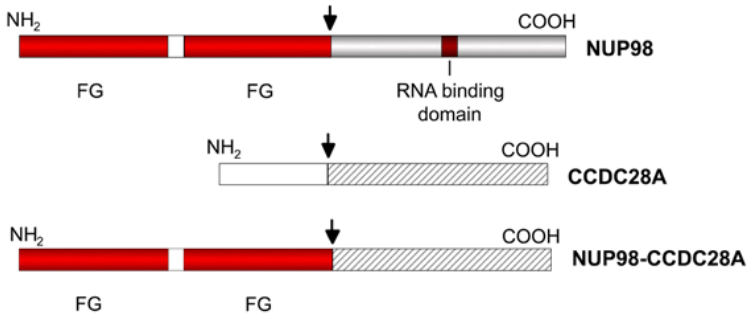
NUP98/CCDC28A

Description

Nucleotide sequence analyses revealed an in-frame fusion between the 13th exon of NUP98 and the second exon of CCDC28A. A reciprocal CCDC28A/NUP98 fusion transcript was detected but is likely devoid of biological activity due to the lack of a predicted fusion protein (Petit et al, 2012).

Fusion protein

NUP98/CCDC28A



Schematic representation of the wild-type NUP98 and CCDC28 products and of the chimeric fusion protein NUP98-CCDC28.

Oncogenesis

In mouse models it has been demonstrated that the enforced NUP98/CCDC28A expression promoted the proliferative and self-renewal capacities of hematopoietic progenitors and rapidly caused fatal myeloproliferative neoplasms and defects in the differentiaton of the erythro-megakaryocytic lineage. Although the leukemogenic mechanism remains unknown, NUP98/CCDC28A retains the NUP98 GLFG-repeats able to associate with core binding protein and/or EP300 and has a nuclear localization suggesting possible transactivation activity. The transformation mediated by NUP98/CCDC28A was not associated with deregulation of the HOXA-Meis1 pathway, a feature shared by a diverse set of NUP98 fusions. Additional investigation will be needed to elucidate the role of NUP98/CCDC28A in lymphoid transformation (Petit et al, 2012).

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